university of groningen

faculty of mathematics and natural sciences

Sleep-wake models

Bachelor Project Mathematics

July 2016

Student: J. J. Staal

First supervisor: Prof.dr. H. Waalkens

Second supervisor: Dr. I. Hoveijn

Sleep-wake models

Jasper Staal
s2330032

First supervisor: H. Waalkens
Second supervisor: I. Hoveijn

May 2016

Abstract

In this thesis we are going to make a comparison between two different sleep models. The two process model is based on a certain "sleep pressure". The stress increases when a person is awake and the stress decreases during sleep. When awake, the stress will reach an upper level and the person will turn to sleep untill a lower bound is reached. However this upper and lower bounds depend on external factors(e.g. day and night) regulated by the internal clock and is a 24 hour periodic function. The other model, the PR model, is also based on a sleep pressure, but now depending on two different brain areas which are active either during sleep or while awake and the interaction between those two areas. This can be represented by a three-dimensional system of differential equations where each equation represent either one of the two brain areas or the sleep pressure. We will obtain a slow-fast system and therefore we are comparing these models by taking the slow time limit and the hard switch limit in the PR model, the concept of these limits will be explained. Furthermore we are going to analyse the dynamics on the slow manifold of the PR model.

Contents

1 Introduction

In this thesis we are going to analyse two different sleep models. The first one, the two-process model, is a model based on the assumption of a sleep pressure. This sleep pressure increases while a person is awake and decreases when a person is asleep. When this pressure reaches a certain upper or lower level, the person will switch to sleep or wake respectively. These upper and lower level are not constant but vary in a 24-hour period regulated by the internal clock. There is some criticism on the model because there is only a little physiological basis for the model. For all that, the model resembles the sleep-wake cycle very well. The other model is the PR-model. It also deals with a sleep pressure, but in this case there are two different brain areas associated with either sleep or wake. The process of falling asleep and waking up is regulated by this dynamical process. Since the increase and decrease in the sleep pressure is a much slower process than the increase and decrease in the potential of the neurons in the brain area, we are dealing with a slow-fast system. This model is described by a system of three differential equations. Taking the hard switch limit and the slow time limit will give us a good way to compare both models.

2 Two process model

As said in the introduction, the two process model [1] is based on a "sleep pressure". When an individual is awake the sleep pressure will increase. In this model there is chosen for an expontential function which converges to a certain level in the limit to infinity, since the sleep pressure can not increase forever. When the individual is asleep the sleep pressure will decrease. Since this can not decrease forever it will also converge exponentialy to a certain lower asymptote in the limit to infinity. The other process switches between wake and sleep. The switch from wake to sleep will occur when a certain upper level is reached and the switching for sleep to wake will occur when a certain lower level is reached. This upper and lower level are not constant, but change during 24 hours by a periodic function regulated by the internal clock. The increase and decrease are described by the following functions respectively:

$$H(t) = \mu + (H_0 - \mu)e^{\frac{t_0 - t}{\chi_w}} \tag{1}$$

$$H(t) = H_0 e^{\frac{t_0 - t}{\chi_s}} \tag{2}$$

Here $H(t)$ is the sleep pressure on a certain time t, H_0 is a "starting point" in the sleep pressure. t_0 is the starting moment. μ is in this case the upper asymptote for the increase of the function. The function is chosen to be an exponential function which converges in the limit to infinity, since H can not have an endless increase or decrease. The function for sleep will converge to zero in the limit. χ_s and χ_w determines the decrease and increase speed of the model respectively.

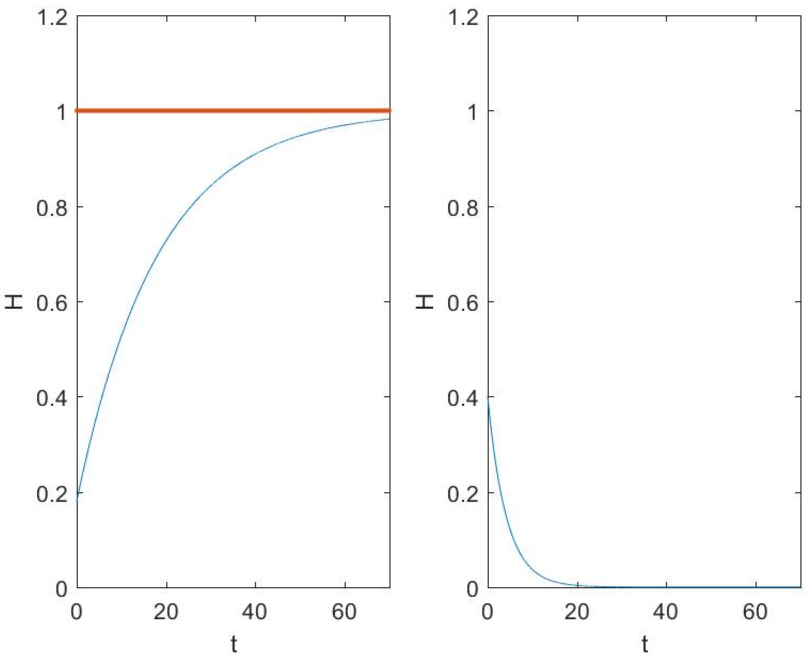

Figure 1 – Left: the sleep pressure while awake with the red line for the value of μ which is the upper asymptote. Right: the sleep pressure while asleep.

Switching from wake to sleep will occur when the pressure H will reach a upper threshold which is described by

$$H^+(t) = H_0^+ + aC(t) \tag{3}$$

This threshold will be reached at a certain moment t1 and on the other hand the switch from sleep to wake will occur when the sleep pressure reaches a lower threshold

$$H^-(t) = H_0^- + aC(t) \tag{4}$$

We will reach this threshold at a certain moment t2. When this moment is reached the process will start all over again. $C(t)$ describes the circadian process and is a periodic function with a period of 24 hours regulated by the internal clock.

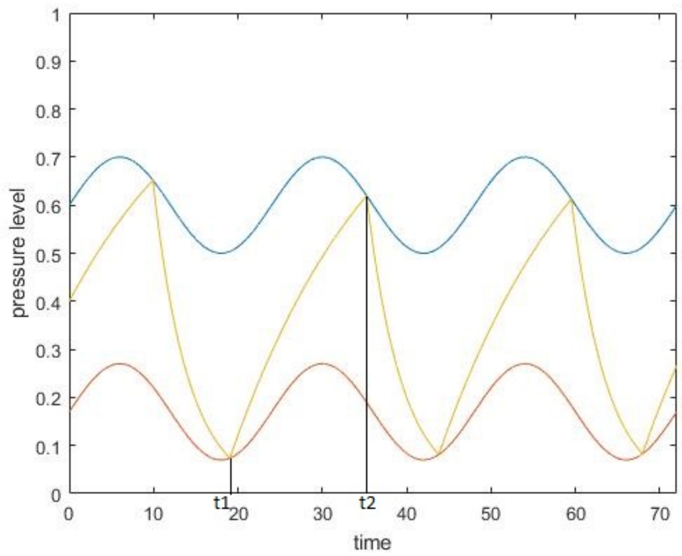

Figure 2 – The two process model plotted for the upper level with $H_0^+ = 0.6$, and the lower level with $H_0^- = 0.18$. t1 and t2 are indicated for the moments of switching.

3 PR model

The PR model as in [3] consists of three processes. Two processes are described by the activity of neurons in two different brain areas. One of this brain areas(MA) is related to wake and the other brain area(VLPO) is related to sleep. The activity of the neurons is determined by the potential. The interaction between these processes is that only one can be active. The activity of one suppress the others activity. The third process is the sleep pressure. If the brain area related to wake is active, the sleep pressure will increase. Also is the internal clock taken into account which influences the brain area related to sleep. We represent the neurons by their mean cell body potential V_v and V_m for VLPO and MA respectively. We can represent the dynamics of the potentails V_v and V_m and the sleep pressure H as in section 2 by:

$$\tau_v \dot{V}_v = v_{vm}Q(V_m) + v_{vc}C + v_{vh}H - V_v \qquad = f_1(V_v, V_m, H) \tag{5}$$

$$\tau_m \dot{V}_m = v_{mv}Q(V_v) + v_{ma}Q_a - V_m \qquad = f_2(V_v, V_m, H) \tag{6}$$

$$\chi \dot{H} = \mu Q(V_m) - H \qquad = f_3(V_v, V_m, H) \tag{7}$$

This is a process in $\mathbb{R}^3$ since we have three variables V_v, V_m and H. Here the v_{ij}'s are parameters which determine the amount of influence each variable gives to the other. C is the 24-hour periodic function which relates to the internal clock as in section 2. Q_a is taken to be constant in this case. The parameters τ_v, τ_m and χ determine how fast the changes in each variable are.

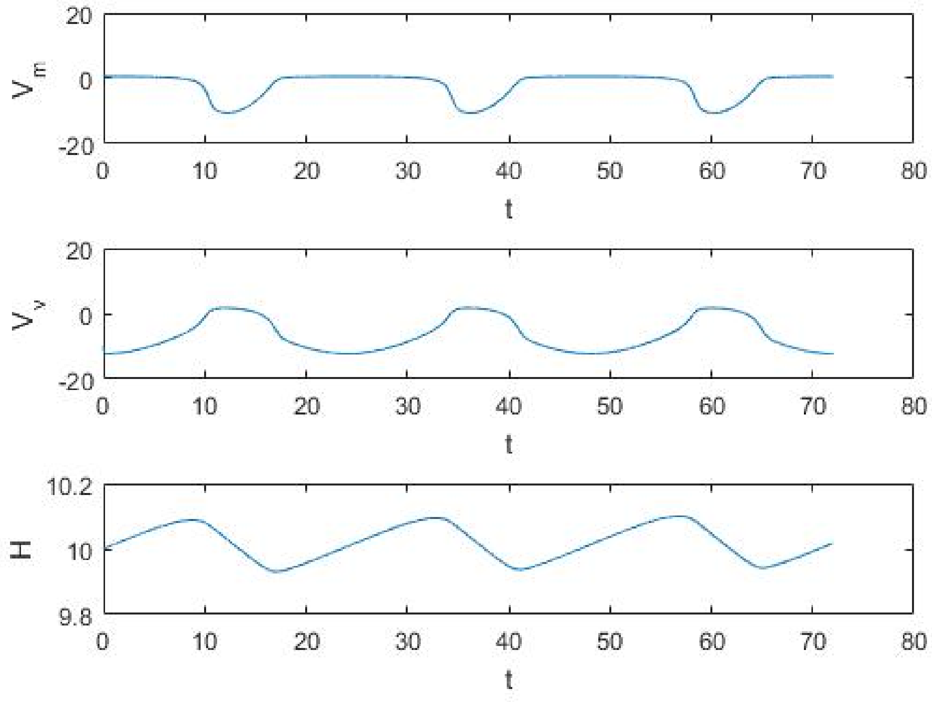

Figure 3 – The PR model for the three parameters plotted against the time.

Q is the firing rate related to the potentials. The interaction between the three processes is depending on this firing rate. We can call it a switch mechanism because this function is a sigmoid function. It will only influence the activity in the neurons if the potential of the neurons in the other brain area is large enough. We describe the firing rate as follows:

$$Q(V_j) = \frac{Q_{max}}{1 + e^{-\frac{V_j(t)-\theta}{\sigma}}} \qquad \text{for } j = m, v \tag{8}$$

Here, Q_{max} is the maximum firing rate and θ is called the mean firing threshold and this θ determines the moment of switching, i.e. when the potential V_j is large enough compared to θ the function firing function will become larger. The parameter σ determines the steepness of the switch. When σ will go to zero we will obtain a step function.

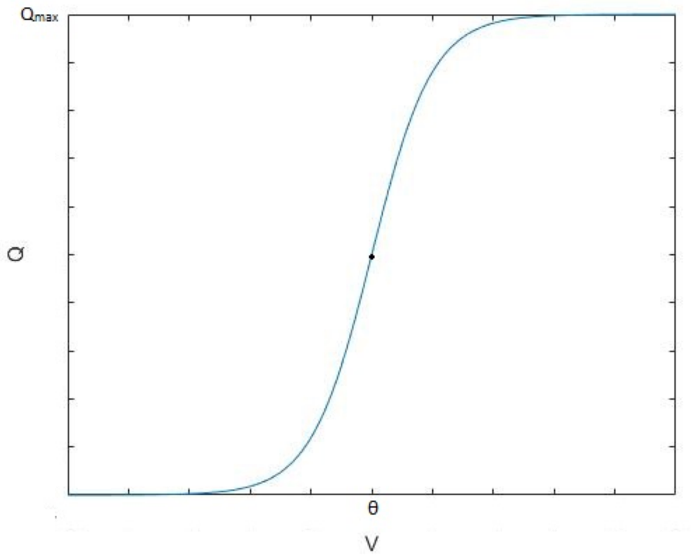

Figure 4 – The firing function Q against the potential V, where θ determines the moment of switching. It approaches a maximum value for the firing rate.

As said before the moment of switching depends on θ. The steepness of the graph depends on the parameter σ so we say that the "hardness" of the switch depends on σ. We can write

$$Q(V_j) = \frac{Q_{max}}{1 + e^{-\frac{V_j(t)-\theta}{\sigma}}} = Q_{max} g(V_j - \theta)$$

where $g(x) = \frac{1}{1+e^{-x/\sigma}}$. If we take the limit $\sigma \to 0$ we will obtain a stepfunction for the firing rate. This stepfunction is called the "hard switch", where $g(x)$ becomes $g(x) = \begin{cases} 1 & \text{if } x \geq 0 \\ 0 & \text{if } x < 0 \end{cases}$

Unless the fact that this firing rate function is discontinuous the system will become much easier.

3.1 Slow-fast system

We know that the process in the brain areas is much faster than the increase and decrease of the sleep pressure. So we are dealing with a so called slow-fast system. We notice that in our system $\tau \ll \chi$. So than we can introduce a small parameter $\epsilon = \frac{\tau}{\chi}$. Now we let $t' = \frac{t}{\epsilon}$ and $T = t$ where t' is the fast time and T is the slow time. Then

$$\frac{d}{dt'} = \frac{d}{dt}\frac{dt}{dt'} = \epsilon \frac{d}{dt}$$

and

$$\frac{d}{dT} = \frac{d}{dt}$$

At slow time our system becomes:

$$\begin{aligned} \epsilon \dot{V}_v &= f_1(V_v, V_m, H) \\ \epsilon \dot{V}_m &= f_2(V_v, V_m, H) \\ \chi \dot{H} &= f_3(V_v, V_m, H) \end{aligned}$$

The slow subsystem, the system where ϵ becomes 0, will then be.

$$
\begin{aligned}
0 &= f_1(V_v, V_m, H) \\
0 &= f_2(V_v, V_m, H) \\
\dot{H} &= f_3(V_v, V_m, H)
\end{aligned}
$$

Hence we get a restriction for V_v, V_m and H. From this restriction we can obtain the slow manifold. This slow manifold is a curve in $\mathbb{R}^3$. Any point away from the slow manifold makes no sense in this system. The dynamics on the slow manifold is described by the function for $\dot{H}$.

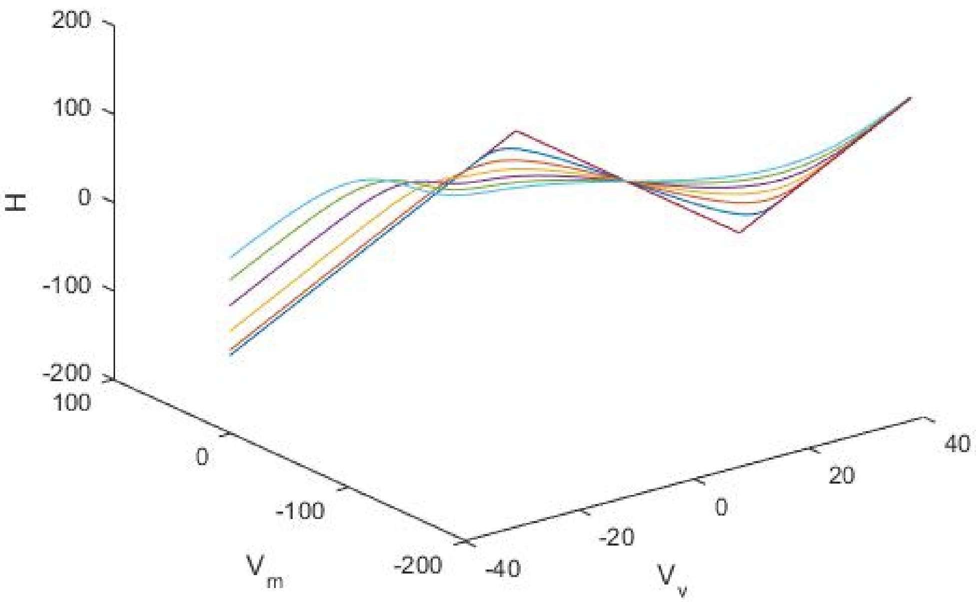

Figure 5 – The slow manifold for different values of sigma in $\mathbb{R}^3$

Rescaling to the fast time system ($t' = \epsilon T$) gives

$$
\begin{aligned}
V_v' &= f_1(V_v, V_m, H) \\
V_m' &= f_2(V_v, V_m, H) \\
H' &= \epsilon f_3(V_v, V_m, H)
\end{aligned}
$$

So the fast subsystem, also called the layer problem, becomes,

$$
\begin{aligned}
V_v' &= f_1(V_v, V_m, H) \\
V_m' &= f_2(V_v, V_m, H) \\
H' &= 0
\end{aligned}
$$

And hence the system will not change in the H-direction, that's why it is also called the layer problem. In the fast subsystem we will move in the plane for constant H.

So comparing the slow and fast time, the limit $\epsilon \to 0$ has a different result in each timescale. If we are dealing with the slow time we will get a restriction for V_v, V_m and H. On the other hand in the fast time starting at a certain point will give us a curve in the V_v, V_m plane with a fixed H since $H' = 0$.

4 Comparison in the slow time limit and the hard switch case

We are going to describe the correspondence between the two process model and the PR model in the slow time limit and the hard switch case. In the two process model we saw that the switching was hard. When an upper level was reached the individual switches immediately from wake to sleep and the other way around when a lower level is reached. We are looking at the slow time limit since the two process model deals with the sleep pressure. Because the sleep pressure changes slow comparing to the changes in the potential.

Now if we take the slow time limit the system becomes:

$$0 = v_{vm}Q_s g(V_m - \theta) + v_{vc}C + v_{vh}H - V_v \quad (9)$$
$$0 = v_{mv}Q_s g(V_v - \theta) + v_{ma}Q_a - V_m \quad (10)$$
$$\chi\dot{H} = \mu Q_s g(V_m - \theta) - H \quad (11)$$

Comparing this in the hard switch limit we will have four cases, namely:

1. $V_m < \theta \quad V_v < \theta$
2. $V_m > \theta \quad V_v > \theta$
3. $V_m > \theta \quad V_v < \theta$
4. $V_m < \theta \quad V_v > \theta$

In the first case, equation (10) becomes $V_m = v_{ma}Q_a$, but since $v_{ma}Q_a$ is chosen to be larger than θ this contradicts the fact that $V_m < \theta$ so this case is inconsistent. In the second case, equation (10) becomes $V_m = v_{mv}Q_s + v_{ma}Q_a$ since $v_m v < 0$ this term becomes smaller than θ and this contradicts the fact that $V_m > \theta$ so also this case is inconsistent.
In case three, which is associated with wake($V_m > \theta > V_v$) this leads to the following:

$$V_v = v_{vm}Q_s + v_{vc}C + v_{vh}H$$
$$V_m = v_{ma}Q_a$$
$$\chi\dot{H} + H = \mu Q_s$$

solving this for H gives us:

$$H = \mu Q_s + (H_0 - \mu Q_s)e^{\frac{T_0 - T}{\chi}}$$

and in the fourth case which is associated with sleep($V_m < \theta, V_v \geq \theta$):

$$V_v = v_{vc}C + v_{vh}H$$
$$V_m = v_{mv}Q_s + v_{ma}Q_a$$
$$\chi\dot{H} + H = 0$$

solving this for H gives us:

$$H = H_0 e^{\frac{T_0 - T}{\chi}}$$

We know that the switch will occur at $V_v = V_m = \theta$ that is when H reaches some upper level H^+ or when H reaches a lower level H^-. We can obtain an expression for the upper and lower level from the equation for V_v. Then

$$H^+ = \frac{\theta - v_{vm}Q_s}{v_{vh}} - \frac{v_{vc}}{v_{vh}}C$$
$$H^- = \frac{\theta}{v_{vh}} - \frac{v_{vc}}{v_{vh}}C$$

And if we look to equation (1),(2),(3) and (4) in section two we observe that the equations that we found for the PR model in the hard switch limit and the slow time limit are the same as in the two process model. Further elaboration of this calculation can be found in appendix C.

5 Slow manifold and the dynamics

As said before we can obtain the slow manifold by setting $\epsilon = 0$ in the slow time limit case. Thus we will obtain a restriction for V_v, V_m and H. So we plotted H as a function of V_m and V_v for different values of σ. This will give us a function in $\mathbb{R}^3$. Away from this slow manifold the slow subsystem makes no sense. The dynamics of this slow subsystem are only defined on the slow manifold.

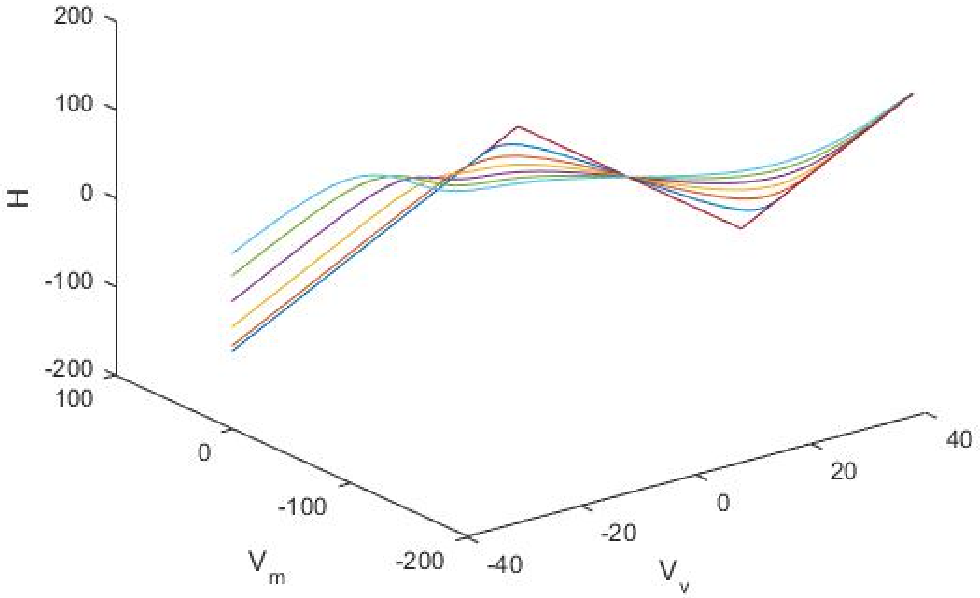

Figure 6 – The slow manifold for different values of sigma in $\mathbb{R}^3$

As we can see in figure 6, the sleep pressure H increases with increasing in the potential V_v. So we can analyse the dynamics on the slow manifold in the hard switch case in the V_v, V_m-plane. In the previous section we had four cases for values of V_v and V_m but we already know two of these cases are inconsistent. Therefore we will only take two of these into account. Then we will define three important points on the slow manifold as H_1,H_2 and H_3. Namely H_1 is the value of H of the point where the switch from wake to sleep occurs. H_2 is the value of H of the point where the switch from sleep to wake occurs and H_3 is the the point where $\dot{H} = 0$ i.e. $H = \mu Q_s$ in the case that V_m is larger than θ and in the case that V_m is smaller than θ, $\dot{H} =$ if $H = 0$. For these two cases we have equilibrium solutions in the plane where H is either equal to zero or equal to μQ_s. So

$$
\begin{aligned}
H_1 &= \frac{\theta - v_{vm}Q_s}{v_{vh}} - \frac{v_{vc}}{v_{vh}}C \\
H_2 &= \frac{\theta}{v_{vh}} - \frac{v_{vc}}{v_{vh}}C \\
H_3 &= \mu Q_s
\end{aligned}
$$

We know that $v_{vm} < 0$ so $H_1 > H_2$. Then we can define three cases, namely:

A. $H_1 > H_2 > H_3$
B. $H_1 > H_3 > H_2$
C. $H_3 > H_1 > H_2$

We are going to describe the dynamics in each case. If we start with a small H, V_v will be small and we will converge towards point H_3. If we start with a large H we will converge to a 0, but since H_2 is larger than 0 we will end up in H_2, switch to wake and so we jump to the other branch and than end up in H_3 again. For the second case, this will be the same. Those two cases make no sense because the meaning is that an individual will stay awake and the sleep pressure does not increase or decrease. This is shown in figure 7.

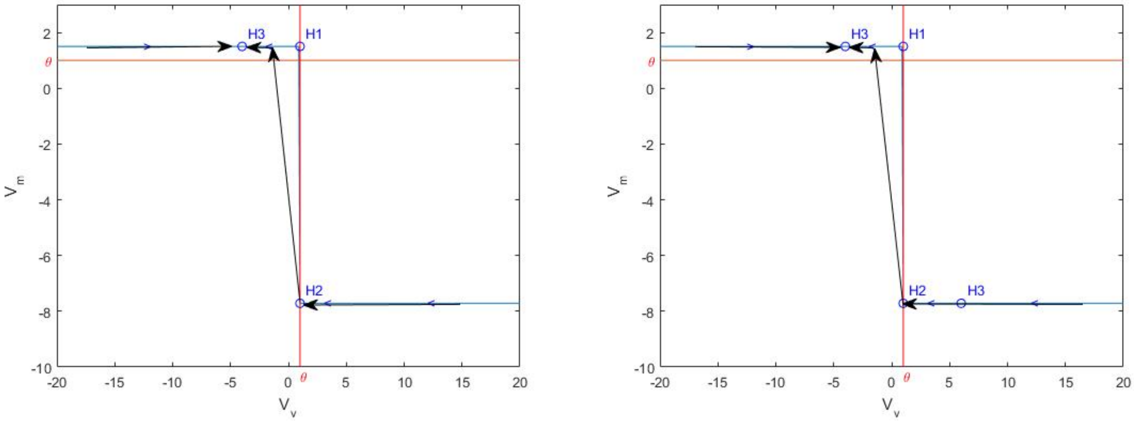

Figure 7 – The dynamics on the slow manifold in case A on the left and case B on the right.

In the third case, the more interesting one, we will end up in H_1 if we start with a small H and then switch to sleep, somewhere inbetween H_2 and H_3 and then end up in H_2 and switch to wake again and so on. So here we see the switching process between wake and sleep. So the system will end up in a limit cycle. The dynamics on the slow manifold can also be seen in figure 8. Hence this is the same process as the two process model, which we have already seen in the previous section for the slow time limit and the hard switch limit.

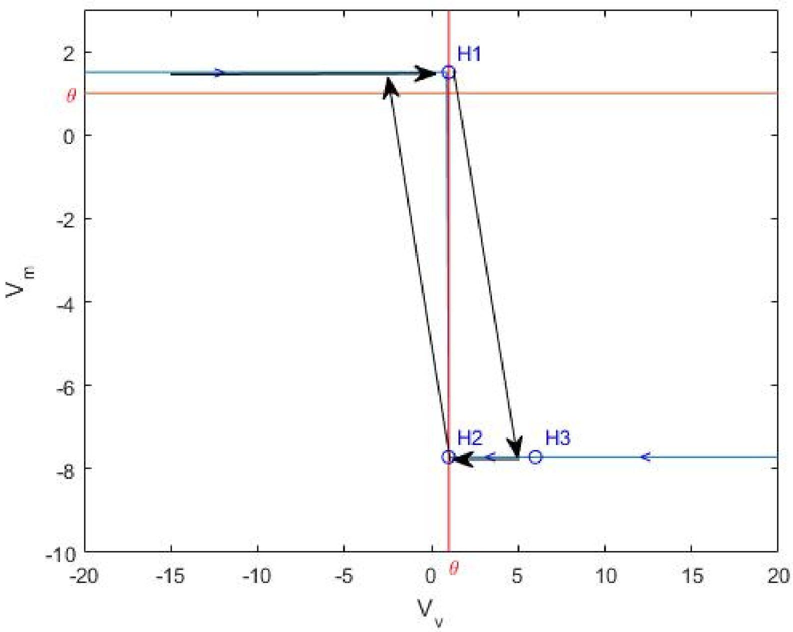

Figure 8 – The dynamics on the slow manifold in case C.

Also in the soft switch case where the function for the firing rate is continuous and differentiable it is possible to find a limit cycle. Namely by finding the points where the system fails to be normally hyperbolic on the slow manifold. It is possible to write H as a function of V_v and V_m, let's say $G(V_v, V_m, H) = H$. Then

$$\nabla G = (0, 0, 1) = \alpha \nabla f_1 + \beta \nabla f_2$$

together with $f_1 = 0$ and $f_2 = 0$ yields five equations and five unknows $\alpha, \beta, V_v, V_m, H$. Solving this will give the points where the system fails to be normally hyperbolic. The linear part of the fast subsystem is described by the functions:

$$V_v' = f_1(V_v, V_m, H)$$
$$V_m' = f_2(V_v, V_m, H)$$

So we know that if there is a point where the system fails to be normally hyperbolic, we will move along the curve described by those two equations towards the slow manifold through the plane for constant H. After that we will reach the slow manifold since H increases to infinity for V_v increasing to infinity so there will be an other point where the slow manifold passes through the same plane. Depending on the choice of σ we see that there are more points where the normal hyperbolicity fails, so we obtain a stable limit cycle for a good choice of the parameters. This describes the sleep-wake process for the case that $\sigma > 0$. See also [2].

6 Conclusion

As we have seen taking the hard switch and slow time limits in the PR model will lead to the expressions for the two-process model. Also we notice this behaviour when we analyse the dynamics on the slow manifold. So we can conclude that the PR model resemble the two-process model when close to the slow manifold. Also as we have seen earlier taking the slow time limit and the hard switch limit shows us the similarity in the PR model and the two-process model. So on first sight the two process model is only based on the assumption of a sleep pressure and the PR model based on the interaction between parts of the brains and activity in these parts and they look very different, but when looking further it gives us a good possibility to compare and see how corresponding the both models are. Also when we take the slow manifold for the case that $\sigma > 0$ we will obtain a limit cycle, so this describes a sleep-wake cycle for the PR-model, but not the same as the two process model since the switching process is not hard, but a differentiable continuous function.

A parameter values for the PR model

Q_{max}	100	sec^{-1}
θ	1	mV
σ	3	mV
$v_{ma}Q_a$	1.5	mV
v_{vm}	-1.9	mV sec
v_{mv}	-1.9	mV sec
v_{vc}	-6.3	mV
v_{vh}	0.19	mV nM^{-1}
χ	10.8	h
μ	10^{-3}	nM h
τ_m	10	sec
τ_v	10	sec

B Matlab codes

B.1 Two-process model

```
t=(0:0.01:72)';
n=length(t);
omega=pi/12;
C=sin(omega*t);
H0s=ones(n,1)*0.75;
H0l=ones(n,1)*0.17;
a=0.1;
mu=1;
t0=0;
chi_s=4.2;
chi_w=18.2;
H0=0.18;
Hu=H0s+a*C;
Hl=H0l+a*C;
Hw=zeros(n,1);
Hs=zeros(n,1);
for i=1:n
Hw(i)=mu+(H0-mu)*exp((t0-t(i))/chi_w);
    if le(Hw(i),Hu(i))
       j=i;
    end
end
while le(i,n)
t0=t(j);
H0=Hw(j);
for i=j:n
Hs(i)=H0*exp((t0-t(i))/chi_s);
Hw(i)=0;
if ge(Hs(i),Hl(i))
    k=i;
end
end
t0=t(k);
H0=Hs(k);
for i=k:n
    Hw(i)=mu+(H0-mu)*exp((t0-t(i))/chi_w);
    Hs(i)=0;
    if le(Hw(i),Hu(i))
       j=i;
```

```
    end
end
i=j+1;
end


H=Hw+Hs;
plot(t,Hu,t,Hl,t,H)
axis([0 72 0 1])
```

B.2 PR model

```
t=0:0.01:72;
x=[-10 1 10];
tau_v=10;
tau_m=10;
chi=10.8*3600;
v_vm=-1.9;
v_vc=-6.3;
v_vh=0.19;
v_mv=-1.9;
v_maQ_a=0.7;
mu=3600*10^-3;
C=(1+cos(pi/12*t))/2;
Qmax=100;
theta=10;
sigma=3;
xArray=zeros(length(t),3);
for i=1:length(t)
    xArray(i,:)=x;
    xprime=[
    1/tau_v*(v_vm*Qmax/(1+exp(-(x(2)-theta)/sigma))+v_vc*C(i)+v_vh
       *x(3)-x(1));
    1/tau_m*(v_mv*Qmax/(1+exp(-(x(1)-theta)/sigma))+v_maQ_a-x(2));
    1/chi*(mu*Qmax/(1+exp(-(x(2)-theta)/sigma))-x(3))];
x=x+xprime';
end
subplot(3,1,2)
plot(t,xArray(:,1))
subplot(3,1,1)
plot(t,xArray(:,2))
subplot(3,1,3)
plot(t,xArray(:,3))
```

B.3 Slow manifold

```
x=(-40:0.1:40);
tau_v=10;
tau_m=10;
chi=10.8*3600;
v_vm=-1.9;
v_vc=-6.3;
v_vh=0.30;
v_mv=-1.9;
v_maQ_a=1.5;
Q_s=4.85;
```

```
mu=3.6;
C=1;
Qmax=Q_s;
theta=1;
Sigma=1:6;
n=length(x);
y=zeros(n,7);
z=zeros(n,7);
Qv=zeros(n,7);
Qm=zeros(n,7);
f=zeros(n,1);
g=zeros(n,1);
Hdot=zeros(n,7);
for j=1:6
    sigma=Sigma(j);
    for i=1:n
    Qv(i,j)=Qmax/(1+exp(-(x(i)-theta)/sigma));
    y(i,j)=v_mv*Qv(i,j)+v_maQ_a;
    Qm(i,j)=Qmax/(1+exp(-(y(i,j)-theta)/sigma));
    z(i,j)=1/v_vh*(x(i)-v_vc*C-v_vm*Qm(i,j));
    Hdot(i,j)=1/chi*(mu*Qm(i,j)-z(i,j));
    end
end
for i=1:n
    if ge(x(i),theta)
        f(i)=1;
    end
    Qv(i,7)=Q_s*f(i);
    y(i,7)=v_mv*Qv(i,7)+v_maQ_a;
    if ge(y(i,7),theta)
        g(i)=1;
    end
    Qm(i,7)=Q_s*g(i);
    z(i,7)=1/v_vh*(x(i)-v_vc*C-v_vm*Qm(i,7));
    Hdot(i,7)=1/chi*(mu*Qm(i,7)-z(i,7));
end

subplot(1,2,1)
plot3(x,y,z)
hold on
plot3(x,y(:,7),z(:,7))
subplot(1,2,2)
plot(x,y(:,7),x,theta*ones(length(x),1),theta*ones(length(x),1),x
    ,'red',theta,[v_maQ_a;v_maQ_a+v_mv*Q_s],'bo',[theta-5;theta
    +5],[v_maQ_a,v_maQ_a+v_mv*Q_s],'bo')
xlabel('V_v')
ylabel('V_m')
text(-21,1,'\theta','Color','red')
text(1,-10.3,'\theta','Color','red')
text(1.5,v_maQ_a+0.5,'H1','Color','blue')
text(1.5,v_maQ_a+v_mv*Q_s+0.5,'H2','Color','blue')
text(1.5-5,v_maQ_a+0.5,'H3','Color','blue')
text(1.5+5,v_maQ_a+v_mv*Q_s+0.5,'H3','Color','blue')
text(-12.5,v_maQ_a+0.05,'>','Color','blue')
text([-2;3;12],[v_maQ_a+0.05;v_maQ_a+v_mv*Q_s+0.05;v_maQ_a+v_mv*
    Q_s+0.05],'<','Color','blue')
axis([-20 20 -10 3])
```

C Calculation in the hard switch limit and the slow time limit

Our system is:

$$\begin{aligned}\tau_v \dot{V}_v &= v_{vm}Q_m + v_{vc}C + v_{vh}H - V_v \\ \tau_m \dot{V}_m &= v_{mv}Q_v + v_{ma}Q_a - V_m \\ \chi \dot{H} &= \mu Q_m - H\end{aligned}$$

First we take the slow time limit ($\epsilon = 0$) and the hard switch limit ($Q_j = Q_s g(V_j - \theta)$) where $g(x) = \begin{cases} 1 & \text{if } x \geq 0 \\ 0 & \text{if } x < 0 \end{cases}$ The system then will become:

$$\begin{aligned}0 &= v_{vm}Q_s g(V_m - \theta) + v_{vc}C + v_{vh}H - V_v \\ 0 &= v_{mv}Q_s g(V_v - \theta) + v_{ma}Q_a - V_m \\ \chi \dot{H} &= \mu Q_s g(V_m - \theta) - H\end{aligned}$$

This is a discontinuous system, so we can distinguish between four theta, but we have already seen that two of the four are inconsistent. Evaluating this during wake($V_m > \theta > V_v$) leads to the following:

$$\begin{aligned}V_v &= v_{vm}Q_s + v_{vc}C + v_{vh}H \\ V_m &= v_{ma}Q_a \\ \chi \dot{H} + H &= \mu Q_s\end{aligned}$$

We will now solve the third equation for H:

$$\begin{aligned}\chi \frac{dH}{dt} &= \mu Q_s - H \\ \int_{H_0}^{H} \frac{dH}{\mu Q_s - H} &= \int_{t_0}^{t} \frac{1}{\chi} dt \\ -ln(\mu Q_s - H) + ln(\mu Q_s - H_0) &= \frac{t - t_0}{\chi} \\ -ln(\frac{\mu Q_s - H}{\mu Q_s - H_0}) &= \frac{t - t_0}{\chi} \\ \mu Q_s - H &= (\mu Q_s - H_0)e^{\frac{t_0 - t}{\chi}} \\ H &= \mu Q_s + (H_0 - \mu Q_s)e^{\frac{t_0 - t}{\chi}}\end{aligned}$$

Since we want to know when the switch will occur, we will look at the moment where $V_v = \theta$. So from the first equation of the system we can write

$$\begin{aligned}V_v &= v_{vm}Q_s + v_{vc}C + v_{vh}H \\ v_{vh}H &= V_v - v_{vm}Q_s - v_{vc}C \\ H &= \frac{\theta - v_{vm}Q_s - v_{vc}C}{v_{vh}}\end{aligned}$$

We will call this upper level H^+ On the other hand. During sleep ($V_m < \theta, V_v \geq \theta$) we have:

$$\begin{aligned}V_v &= v_{vc}C + v_{vh}H \\ V_m &= v_{mv}Q_s + v_{ma}Q_a \\ \chi \dot{H} + H &= 0\end{aligned}$$

solving this for H gives us:

$$\begin{aligned}
\chi\frac{dH}{dt} &= -H \\
\int_{H_0}^{H}\frac{dH}{H} &= -\int_{t_0}^{t}\frac{1}{\chi}dt \\
ln(H) - ln(H_0) &= \frac{t_0 - t}{\chi} \\
ln(\frac{H}{H_0}) &= \frac{t_0 - t}{\chi} \\
H &= H_0 e^{\frac{t-t_0}{\chi}}
\end{aligned}$$

And the same as before we can find the lower level from the first equation of the system which is:

$$\begin{aligned}
V_v &= v_{vc}C + v_{vh}H \\
v_{vh}H &= V_v - v_{vc}C \\
H &= \frac{\theta - v_{vc}C}{v_{vh}}
\end{aligned}$$

This lower level will be called H^-

References

[1] S. Daan, D. G. Beersma, and A. A. Borbely. Timing of human sleep: recovery process gated by a circadian pacemaker. *American Journal of Physiology*, 246:161–178, 1984.

[2] R. Haiduc. *A fifty minute introduction to slow-fast systems.* Cornell University, Ithaca, 2004.

[3] A. J. K. Philips and P. A. Robinson. A quantitative model of sleep-wake dynamics based on the physiology of the brainstem ascending arousal system. *Journal of Biological Rhythms*, 22:167–179, 2007.

[4] A. C. Skeldon, D. Dijk, and G. Derks. Mathematical models for sleep-wake dynamics: Comparison of the two-process model and a mutual inhibition neuronal model. *PLoS ONE*, 9(8), 2014.